Remarks/Arguments

Summary of Amendments

Applicants have amended independent claim 1 to limit the claim to a casein fragment being a casein phosphopeptide. Claims 7 and 8 have been rewritten to reflect the dependency on casein phosphopeptide. Claim 9 has been re-written to independent claim form to more clarify the claimed composition as including at least one casein fragment and at least one of a phosphopeptide, a glycopeptide, a glyceride and combinations thereof, which are operable to inhibit oxidation of lipids in oil-in-water or water-in-oil emulsions. Claims 3, 5, 11, 12, 14, 15, 17, 18, 20, 43, 44, 47-49, 65-66 have been rewritten to achieve more precise clarity. Claim 42 has been rewritten to reflect the utilization of a casein fragment as opposed to a casein phosphoprotein. Claims 47-53 have been amended in their dependency to depend from independent Claim 1, or an intervening claim, rather than from canceled Claims 21-41. Claims 10, and 50-53 have been amended in their dependency to depend from independent claim 9. Claims 54-64, which were withdrawn by the Examiner as being directed to the non-elected claims of Group II, have been canceled.

Summary of Examiner's Action:

The Examiner has rejected the claims as follows:

1. Claims 1-3, 6-7, 9, 16-18, 20, 42-44 and 65-66 under 35 U.S.C. §102(b) as allegedly being anticipated by Kahn, et al.;
2. Claims 4-5, 8 and 10-12 under 35 U.S.C. §102(b) or, alternatively, under 35 U.S.C.103(a) over Kahn, et al.;
3. Claims 14-15 under 35 U.S.C. §103(a) as being obvious over Kahn in view of Musher;
4. Claims 1-3, 6-7, 9, 14, 16-18, 20, 42-44 and 65-66 under 35 U.S.C. §102(b) as begin anticipated by DeMichele, et al.;

5. Claims 4-5, 8, 10-12 and 15 under 35 U.S.C. §102(b) as being anticipated by, or alternatively, under 35 U.S.C. §103(a) as being obvious over DeMichele;
6. Claims 1, 6-9, 14, 16-18, 20, 42-44 and 65-66 under 35 U.S.C. §102(b) as being anticipated by Musher;
7. Claims 4-5, 10-12 and 15 under 35 U.S.C. §102(b) as being anticipated by, or alternatively under 35 U.S.C. as obvious over Musher, optionally in view of Buikstra, et al.; and
8. Claims 2-3 under 35 U.S.C. §103(a) as being obvious over Musher in view of DeMichele or Kahn.

Khan is cited as teaching freezer stable whipped ice cream and milk shake food products. The Examiner relies upon Examples 1-2 of Khan which, the Examiner alleges, comprise in part: nonfat dry milk as a source of casein, with casein comprising phosphopeptides, sucrose (a non-reducing sugar), Seakem C, a calcium carrageenan, which comprises a sulfated polysaccharide), D-23-A (a source of Dutch cocoa powder), soybean and coconut oils (sources of highly unsaturated oils), etc.

The Examiner further alleges that while it is unclear from Khan whether Examples 1-2 teach medium-chain triglycerides, or the specific claimed casein components, the Examiner argues that it would have been obvious to use medium-chain triglycerides in the food products of Kahn since

> such medium-chain triglycerides are deemed to be a component found within soybean oils and/or coconut oils. In any case medium-chain triglycerides are well known fats used in all sorts of edible food emulsions in the art. Further, applicants' claimed casein type components are deemed to be obvious over the disclosure of Khan et al because such caseins are known components of milk and would thus be obvious to use in Khan et al's freezer stable whipped ice cream and milk shake products.

Examiner's 7/18/2005 Office Action, p. 4.

Musher is cited by the Examiner as purportedly teaching stabilization of food type water and oil emulsions containing highly unsaturated oils by using 1) a sugar (e.,

sucrose, maltose, lactose), 2) non-aromatic nitrogen compounds such as casein (which comprises phosphopeptide units) or gelatin (which comprises phosphopeptide units), and/or phosphatide = phospholipids (e.g., lecithin and cephalin) and 4) optional other adjuvant.

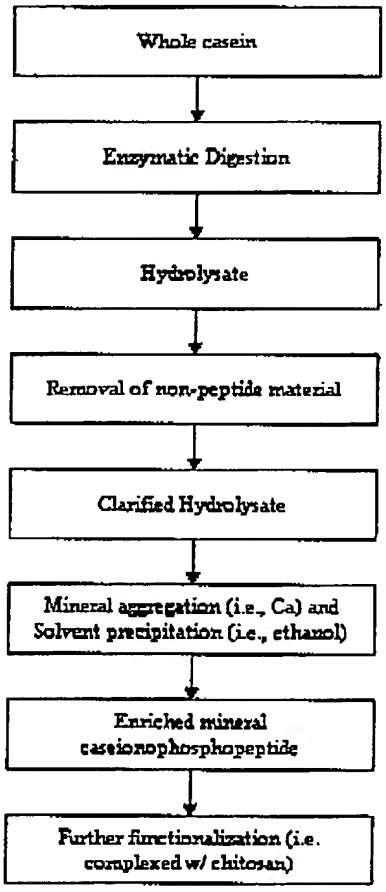
DeMichele is cited as teaching nutritional food products in the form of emulsions containing unsaturated oils, non-reducing sugars (e.g., sucrose), acid casein and calcium caseinate (both comprising phosphophopeptides), lecithin (comprising phospholipids), carrageenans (which comprise sulfated polysaccharides), etc. In support of this interpretation of DeMichele, the Examiner references the Abstract, and Col. 16, line 56 to Col. 17, line 61. The Examiner also cites Table 8 of DeMichele as teaching medium-chain triglycerides which are deemed to be a component within Borage oil, fish oil, MCT oil, and/or canola oil, as teaching applicant's casein components, and as broadly disclosing the use of phopspolipids derived from egg yolks or soybeans.

Phosphoproteins and Not Phosphopeptides.

The Examiner comments with respect to Applicants' remarks in response to the First Office Action are well-taken. However, in view of the following remarks, Applicants assert that the pending claim patentably distinguish over the art cited and of record.

At the outset, it is critical to understand the distinction between ***phosphoproteins*** and ***phosphopeptides***. The Examiner has apparently used these terms synonymously, when, in fact, they are not synonymous nor are they understood by those in the art as being synonymous. ***Phosphoproteins*** are defined as "Any of a group of proteins, such as casein, containing chemically bound phosphoric acid." The American Heritage_ dictionary of the English Language, *Fourth Edition, Copyright 2000 by Houghton Mifflin Company. The American Heritage Stedman's Medical Dictionary. Copyright 2002, 2001, 1995* by Houghton Mifflin Company. Found at www.dictionary.com.

Phosphopeptides, on the other hand, are ***peptides*** which are the product of *protein digestion*. For example, phosphopeptides are peptides produced during the course of digesting proteins with endoproteases. The distinction between the phosphopeptide and the protein from which it is derived is well-known by those skilled in the art, including the distinction between casein proteins and casein phosphopeptides. Casein phosphopeptides are prepared by enzymatic hydrolysis of casein with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol (see figure below).



Also note that the preparation, as referenced by the American Dairy Products Institute http://www.adpi.org/product_drymilk.asp?catid=2&pid=2 link , of nonfat dry milk is simply prepared by the removal of water as paraphrased "Nonfat dry milk is white to light cream in color with a clean dairy flavor. It is manufactured by removing water from pasteurized skim milk."

The caseins can be subdivided into four types, i.e., α_{s1}-casein, α_{s2}-casein, β-casein, κ-casein, a classification based on their different mobilities during electrophoresis in alkaline urea polyacrylamide gels. Phosphorous is bound to the caseins via monoester linkages to seryl residues. The extent of phosphorylation is dependent on casein type, i.e., bovine α_{s2}-casein can have up to 13 phosphate groups, whereas κ-casein has only one phosphate group. The most abundant protein found in ruminant milk is casein. The casein content of ruminant milk represents about 80% of the total milk proteins. The composition of casein from the milk of cows consists on average of 39.5% α_{s1}-casein, 12.1% α_{s2}-casein, 37.2% β-casein, and 11.2% κ-casein. In the case of casein from the milk of goats characterized by a high α_{s2}-casein content, the percentage composition is as follows: 5.9% α_{s1}-casein, 29.2% α_{s2}-casein, 50.5% β-casein, and 14.4% κ-casein. The distinguishing property of the caseins is their low solubility at pH 4.6. The common compositional factor is that caseins are conjugated proteins, most with phosphate group(s) esterified to serine residues. These phosphate groups are important to the structure of the casein micelle. The conformation of caseins is much like that of denatured globular proteins. The high number of proline residues in caseins causes particular bending of the protein chain and inhibits the formation of close-packed, ordered secondary structures.

Caseins contain no disulfide bonds. As well, the lack of tertiary structure accounts for the stability of caseins against heat denaturation because there is very little structure to unfold. Without a tertiary structure there is considerable exposure of hydrophobic residues. This results in strong association reactions of the caseins and renders them insoluble in water, as cited by See, e.g., www.foodsci.uoguelph.ca/dairyedu/chem.html. As distinguished from the precursor

phosphoproteins, phosphopeptides (i.e., casein phosphopeptides) are the reaction products of enzymatic hydrolysis of such phosphoproteins (i.e., casein) with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol. It is noteworthy to mention here that the "Freezer Stable Whiped Ice Cream and Milk Shake Food Products" of Kahn et al (U.S. Patent No. 4,421,778) is being prepared with Nonfat Milk Solids which only contain casein and whey proteins but do not contain casein phosphopeptides which are hydrolysis products of casein prepared by digestion with the enzyme trypsin with subsequent aggregation with calcium chloride and precipitation with ethanol (as mentioned in our Patent Application). See Claim 1 (Currently Amended). Again, note the production of nonfat dry milk issued by the American Dairy Products Institute (Chicago, IL).

Enzymatic hydrolysis of the different individual caseins, in particular α_{S1}-casein and β-casein, which are characterized by molecular weights of around 32,500 daltons (α_{S1}-casein) and around 24,500 daltons (β-casein) by endoproteinase digestion (i.e., trypsin, chymotrypsin) with subsequent aggregation with calcium chloride and precipitation with ethanol produces smaller fragments with molecular weights of about 4,552 daltons (α_s-casein fragment) and about 3,123 daltons (β-casein fragment). These fragments (or peptides) are produced in vitro by tryptic or chymotryptic fragmentation of these individual caseins. Currently amended Claim 7 of Applicants' Patent Application clearly states that the casein phosphopeptide is selected from the group consisting of alpha-casein, beta casein, kappa-casein, fragments thereof, and any combinations. Claim 8 (Currently Amended) clearly states "the composition of Claim 1, wherein the casein phosphopeptide comprises a caprine casein phosphopeptide". Claim 9 (Currently Amended) clearly states " an antioxidant composition comprising at least one casein fragment, and at least one of a phosphopeptide, a glycopeptide, a glyceride and combination thereof, in an oil-in-water or a water-in-oil emulsion". Claim 10 (Currently Amended) clearly states "the composition of Claim 9, wherein the casein fragment is characterized by a content of alpha.sub.s2-casein greater than 15 percent of total casein and medium-chain triglycerides".

Claim 11 (Currently Amended) clearly states "the composition of Claim 10, wherein the phosphopeptide comprises a caseinophosphopeptide". Claim 12 (Currently Amended) clearly states "the composition of Claim 11, wherein the caseinophosphopeptide comprises a caprine caseinophosphopeptide".

The Khan Reference Fails to Establish prima facie Unpatentability.

The Examiner's reliance upon Kahn as teaching nonfat dry milk as a source of casein which allegedly comprises phosphopeptides is chemically incorrect. Phosphopeptides are low molecular weigh, peptides Milk contains whole casein and its individual casein types (i.e., α_{s1}-casein, α_{s2}-casein, β-casein, κ-casein) which are termed phosphoproteins, but not phosphopeptides which are hydrolysis products of casein prepared by digestion with the enzyme trypsin with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol as mentioned in our Patent Application (see Claim 1 (Currently amended) and Claims 47-51 (Currently amended). In short, to obtain phosphopeptides from casein, one must engage in the enzymatic hydrolysis of whole casein, or its individual casein types (i.e., α_{s1}-casein, α_{s2}-casein, β-casein, κ-casein) with trypsin with subsequent aggregation with calcium chloride and precipitation with ethanol to derive caseinophosphopeptides (i.e., casein phosphopeptides, α_{s2}-casein phosphopeptides or fragments, β-casein phosphopeptides or fragments).

The pending Claims, as amended, claim casein phosphopeptides in either an oil-in-water or water-in-oil emulsion (Claims 1-8, 14-20, 47-53) or casein fragments in a water-in-oil or oil-in-water emulsion (Claims 9-13, 65), and, in the dependent claims, in combination with phosphopeptide, glycopeptide, glyceride or medium-chain triglyceride. The Examiner's reliance upon Khan as anticipatory reference under 35 U.S.C. §102(b), or in the alternative, as primary reference in support of an obviousness rejection under 35 U.S.C §103(a), is inappropriate.

The Khan reference itself, manifestly refutes the Examiner's position that the nonfat dry milk of Examples 1 and 2 teach the use of phosphopeptide, particularly casein phosphopeptide, in an oil-in-water or water-in-oil emulsion. At Col. 5, lines 46-55, Khan

expressly teaches that ***Protein*** concentrates and isolates are useful.....to facilitate and maintain a whipped structure.....milk powder and food ***proteins*** are all useful, generally in concentrations from about 0-10% preferably from about 0.3-3%. Alternatively, use can be made of a protein such as **sodium** or ***calcium caseinate***..... [Emphasis added]

Thus, Khan teaches only the addition of proteins (from the nonfat dry milk and the whey protein concentrate in Example 1 and Example 2 to the emulsion, not phosphopeptides as asserted by the Examiner.

Applicants acknowledge that Example 1 in Khan teaches the use of nonfat dry milk (as a protein source, and not a phosphopeptide source), whey protein concentrate (as a protein source, and not a phosphopeptide source), sucrose (a non-reducing sugar), Seakem C (a refined calcium carrageenan), D-23-A (Dutch cocoa), soybean oil (an unsaturated oil), and coconut oil (a saturated oil). Example 2 teaches the use of nonfat dry milk (as a protein source, not as a phosphopeptide source), in combination with whey protein concentrate (as a protein source, and not a phosphopeptide source), sucrose (a non-reducing sugar), Seakem C (a refined calcium carrageenan), D-23-A (Dutch cocoa), and butter (a saturated fat). However, the mere teaching that milk proteins either in the form of casein such as calcium caseinate, sodium caseinate or whey protein concentrate (or whey protein isolate) is used, in a composition, falls far short of teaching or rendering obvious the use of casein phosphopeptides, which must be obtained by hydrolyzing casein or its individual casein types (i.e., α_{s1}-casein, α_{s2}-casein, β-casein, κ-casein) with endoproteinases with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol. Thus, both the claim composition comprising individual casein fragments, in particular α_{s2}-casein and β-casein fragments, and/or casein phosphopeptides cannot be rendered unpatentable under either §102(b) or §103(a) by the mere disclose of nonfat dry milk protein, without further teaching or suggesting that the protein source has previously being subjected to enzymatic proteolysis (i.e., the use of the enzymes trypsin or chymotrypsin) with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol to yield the casein fragments or casein

phosphopeptides. Kahn neither teaches nor suggest any similar processing of the nonfat dry milk in Examples 1 and 2.

Accordingly, Applicant respectfully submits that Kahn is both inappropriate anticipatory reference under 35 U.S.C. §102(b) and an inappropriate primary reference under 35 U.S.C. §103(a). Withdrawal of the rejections of record based in whole or in part upon Khan is respectfully solicited. Applicant submit, therefore, that each of the pending claims are patentable over Khan.

The DeMichele Reference Similarly Fails to Establish prima facie Unpatentability.

The DeMichele reference, like the Khan reference discussed above, is incorrectly cited both as an anticipatory reference under §102(b) and as a primary obviousness reference under §103(a). Like the Khan reference, DeMichele is cited as teaching a composition including acid casein and calcium caseinate. Both acid casein and calcium caseinate are proteinaceous precipitates from a reaction between acid (1 N HCl) or $CaCl_2$ (2% w/v) and skim milk, respectively. Contrary to the Examiner's assertion, neither are ***casein phosphopeptides*** and neither are ***individual casein fragments*** (i.e., α_s-casein fraction, β-casein fraction, κ-casein fraction) as claimed in the pending claims. The mere presence of an acid-processed casein (i.e., acid casein, but not an enzymatically processed casein with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol) or a calcium-precipitated casein (i.e., calcium caseinate, but not an enzymatically processed casein with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol) in a composition, such as that in DeMichele, neither expressly teaches, nor impliedly suggests to one of ordinary skill in the art (and therefore is devoid of any motivation), that is either known or obvious to substitute phosphopeptides or casein fragments in the manner claimed, for the acid casein or calcium caseinate taught by DeMichele.

The mere fact that DeMichele may teach other claimed components, such as lecithin, carrageenan or non-reducing sugars, wholly fails to make the reference appropriate as an anticipatory or obviousness reference in the absence of a teaching that it

is known or obvious to use *phosphopeptides* or casein fragments in an oil-in-water or water-in-oil emulsion as claimed in Applicants pending claims.

The Musher Reference also Fails to Establish prima facie Unpatentability.

Musher is cited by the Examiner principally because it teaches using casein or gelatin in a composition to stabilize glyceride oils. Like Khan and DeMichele, discussed above, neither casein nor gelatin comprises *phosphopeptide* units as alleged by the Examiner. Rather, casein and gelatin comprise *phosphoproteins*, not phosphopeptides. Again, *phosphopeptides* are the hydrolytic reaction products after reacting the *phosphoproteins* with trypsin with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol. There is no suggestion or teaching in the Musher reference, either express or implied, which would teach the artisan to employ *phosphopeptides* in the oil stabilization mixture disclosed in the reference. Additionally, Musher teaches stabilization of *oils* against oxidative deterioration, *not of oil-in-water or water-in-oil emulsions* as claimed in the present invention, wherein it states:

> Numerous foods contain lipids dispersed in water as membrane bilayers or emulsion droplets. The fact that oxidative reactions in dispersed lipids (or emulsions) are mechanistically different from bulk oils. One of the potential mechanisms that differs in the bulk and emulsified oils is the large surface area of the emulsified lipids, which presents a situation in which water-soluble prooxidants can readily interact with lipids.

Accordingly, Applicant respectfully submits that Musher is both inappropriate anticipatory reference under 35 U.S.C. §102(b) and an inappropriate primary reference or secondary reference under 35 U.S.C. §103(a). Withdrawal of the rejections of record based in whole or in part upon Musher is respectfully solicited. Applicants submit, therefore, that each of the pending claims are patentable over Musher.

The Buikstra Reference Teaching if Insufficient to Establish prima facie Unpatentability Without an Appropriate Primary Reference.

Buikstra is cited only as a secondary reference in combination with Musher. Without a proper primary reference, the teachings of Buikstra, inherently cannot render obvious the presently claimed invention. Thus, it is not necessary to respond to the merits of the Buikstra teaching unless and it is cited with a supporting primary reference. However, it should be noted here that Buikstra et al. teaches the use of hydrolyzed protein (i.e., casein, whey proteins, soybean protein, wheat protein) prepared either by enzymatic hydrolysis or by using other known hydrolytic technique (i.e., acid hydrolysis, basic hydrolysis, or thermal hydrolysis) and hydrolyzed lecithin to produce heat-stable oil-in-water emulsions and not oxidative stable oil-in-water emulsions (See currently amended Claim 1). Heat-stable emulsions refer to enhanced stability towards heat in terms of oil and water phase separation, and decreased formation of sediment (proteinaceous particles). See Examples 2-9 of Buikstra et al. Also, the enzymatically hydrolyzed casein mentioned on the U.S. Patent by Buikstra et al. is not a casein phosphopeptide. A casein phosphopeptide is an enzymatically processed casein with subsequent aggregation with calcium chloride ($CaCl_2$) and precipitation with ethanol.

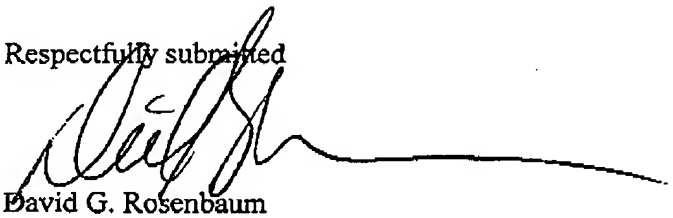
Summary

Accordingly, Applicant submits that the pending claims are patentably distinct from and over the art cited and of record. Favorable reconsideration of the rejection of the pending claims is solicited.

This Amendment is being concurrently filed with an Amendment Transmittal Letter including a fee calculation sheet, any applicable Request for Extension, and fee calculations. The Director is authorized to deduct any additional expenses from Deposit Account No. 18-2000, of which the undersigned is an authorized signatory.

Should the Examiner find that there are any outstanding matters which are susceptible of resolution by telephone interview, the Examiner is invited to telephone the undersigned to discuss the same.

Respectfully submitted



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